

August 1, 1952

Mr. Philip E. Hartman  
Biological Laboratory  
Long Island Biological Association  
Cold Spring Harbor, L.I., N.Y.

Dear Mr. Hartman:

Thank you for your letter of July 29.

Concerning the biochemistry of divers resistant mutants, I have been in correspondence with Dr. Colwell for some time. She is having some difficulty in reproducing her published experiments, but this seems to be a matter of the purity of the reagent, a point not previously emphasized. I am looking forward to a satisfactory confirmation of her experiments (which, *prima facie*, might still very well represent a selection of mutants. Quinones seem to behave very much like penicillin in the selection of auxotrophs in minimal medium).

Our experiments with streptomycin-resistance included an examination of the Merck strain of *E. coli*. They had lost their described non-aerobic  $S^R$  mutant, and neither they nor I have been able to repeat the experiment, even starting with their culture. I do not doubt that there may be biochemical differences among  $S^R$  mutants, and it would certainly be worthwhile to study such mutants before they are exposed to streptomycin. Whether an  $S^R$  mutant is resistant to streptomycin in a non-streptomycin environment is a nearly metaphysical question. The mutant character can only be defined operationally, namely that 100% of the mutant cells survive when they are exposed to SM, whereas almost all non-mutant cells fail to develop. I do not doubt there may be physiological adjustments to the presence of SM when an  $S^R$  cell is exposed to it, but there is no evidence that such exposure induces specific genetic changes.

I would be very much interested to receive further details of the Cu/induced small colony variants, and Dr. DeLamater's new techniques. *E. coli* certainly is very near the limit of useful microscopical techniques.

Sincerely,

Joshua Lederberg